

Application of the McDonald MRI Criteria in Multiple Sclerosis[†]

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Abstract

Introduction: The aim of this study was to assess the sensitivity of McDonald's magnetic resonance imaging (MRI) criteria for the diagnosis of multiple sclerosis (MS) in a group of Asian patients diagnosed with clinically definite MS, based on lesion characterisation on MRI scans. **Materials and Methods:** Forty-nine patients from 3 major neurological institutions were classified as having Asian- or Western-type MS based on clinical assessment. Each MRI scan was reviewed by 2 neuroradiologists for the presence and characteristics of brain and spinal lesions. The McDonald's MRI criteria were then applied and its sensitivity evaluated. **Results:** Nine patients were excluded, leaving 34 females and 6 males who were dominantly Chinese (90%), with a mean age of 36.2 years. The MRI brain and spinal findings were detailed and tabulated. Statistically significant differences ($P < 0.01$) in MRI brain findings and sensitivity of McDonald's MRI criteria were found between our Asian- and Western-type MS patients. The diagnostic yield of McDonald's MRI criteria increased by 20% when we substituted a cord for a brain lesion, and applied the substitution for enhancing cord lesions as well. **Conclusion:** The diagnosis is more likely to be made when using McDonald MRI criteria based on brain findings, in a patient who presents clinically with Western-type MS. The provision for substitution of "one brain for a spinal lesion" is helpful in Asian-type MS, where there is preponderance of spinal lesion load. Our findings suggest that minor modifications in the interpretation of McDonald's MRI criteria have significant impact on the diagnosis in patients clinically presenting as Asian-type MS, with potential bearing on their subsequent management.

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Key words: Asian, Brain, Spinal cord, Western

Introduction

Since its advent in 1982, magnetic resonance imaging (MRI) has become an important component in the evaluation of multiple sclerosis (MS). MRI is a highly sensitive tool for MS, with 95% patients with clinically definite MS (CDMS) demonstrating brain abnormalities.¹ However, MRI is also known to be low in specificity, with a variety of diseases causing MS-like abnormalities in the brain.² Over the years, various composite MR features have been proposed^{1,3,4} to enhance the specificity of MRI for the diagnosis of MS. Most recently, the International Panel on MS Diagnosis⁵ has proposed using MRI as an objective tool to document dissemination in time and space, and

directly incorporating the MRI findings into the overall diagnostic scheme for MS. Their proposed McDonald's MRI criteria were chiefly based on a modification of Barkhof's criteria⁴ and recommendations by Tintore et al.⁶

Since then, various groups⁷⁻¹⁰ have reported the clinical utility of the McDonald's criteria⁵ for the prediction of conversion of clinically isolated demyelinating syndrome to CDMS in a predominantly Western population. However, the utility of the McDonald's MRI criteria in an Asian population has not been formally evaluated.

MS in Asians may present in any of 2 clinical subtypes: Asian- or Western-type MS.^{11,12} Asian-type MS is clinically characterised by a distinctive predilection for severe optic-

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spinal involvement, whereas Western-type MS presents with signs of disseminated central nervous system involvement like that commonly found in the white population.

A diagnosis of MS in an Asian population is not always easy to make, given the relative low prevalence of the condition in this region.^{12,13} This is compounded by the lack of specificity of T2 hyperintense lesions on brain MRI scans,^{2,3} and atypical presentations. Yet, there is clearly a need to make an early diagnosis since various clinical trials have shown the ability to reduce disability and delay onset of MS when treatment is started early for clinically isolated demyelinating syndrome.¹⁴ In addition, the treatment for MS is expensive. Thence, the neuroradiological assessment plays an important role in helping the clinician make the diagnosis in an Asian patient, and the proposed McDonald's MRI criteria for MS⁵ is much welcomed.

The aim of this study was to retrospectively evaluate the sensitivity of McDonald's MRI criteria for the diagnosis of MS in a group of Asian patients clinically diagnosed with CDMS.¹⁵

Materials and Methods

Patients

Patients were recruited from the 3 major neurological institutions in the country, with no restriction on age or disability. The patients included had a diagnosis of CDMS, and were seen at the neurological clinics of the 3 major hospitals over a 5-year period. Careful chart review was further made by the neurologists of this study group to confirm the clinical diagnosis of CDMS, as defined by Poser et al.¹⁵ Only patients with a relapsing-remitting disease course were included in this study. Patients who had positive vascular risk factors (such as coronary heart disease and hyperlipidaemia) or who were positive for markers of an underlying collagen vascular disorder were excluded from the study. Patients whose main lesions based on clinical assessment, were confined to the optic nerve and spinal cord with none localising to the cerebrum or cerebellum, were classified as having Asian-type MS.¹¹ The rest of the MS patients who clinically showed multiple sites of involvement in the central nervous system, including

Table 1. Comparison of MRI Brain Findings Between Western and Asian Types of MS^{11,12}

MRI brain findings	First MR scan			Cumulated scans		
	Total MS (n = 40)	Western MS (n = 14)	Asian MS (n = 26)	Total MS (n = 40)	Western MS (n = 14)	Asian MS (n = 26)
Periventricular lesions						
None	11/40 (28%)		9 (23%)			
3 or more	22 (55%)	11/14 (79%)	11/26 (42%) ^a	27 (68%)	12/14 (86%)	15/26 (58%)
9 or more	14 (35%)	8/14 (57%)	6/26 (23%) ^a	18 (45%)	10/14 (71%)	8/26 (31%) ^b
Corpus callosum	18 (45%)	10/14 (71%)	8/26 (31%) ^b	22 (55%)	11/14 (79%)	11/26 (42%) ^a
Juxtacortical lesions	26 (65%)	11/14 (79%)	15/26 (58%)	29 (73%)	13/14 (93%)	16/26 (62%) ^a
Other white matter lesions						
Internal capsule	11 (28%)	7/14 (50%)	4/26 (15%) ^b	17 (43%)	10/14 (71%)	7/26 (27%) ^c
External capsule	6 (15%)	5/14 (36%)	1/26 (4%) ^c	8 (20%)	7/14 (50%)	1/26 (4%) ^d
Temporal lobe	14 (35%)	8/14 (57%)	7/26 (27%)	23 (58%)	11/14 (79%)	12/26 (46%) ^a
Large lesions (>2 cm)	3 (8%)	3/14 (21%)	0 (0%) ^b	6 (15%)	6/14 (43%)	0 (0%) ^d
Cortical lesions	0 (0%)			4 (10%)	3/14 (21%)	1/26 (4%)
Basal ganglia	7 (18%)	3/14 (21%)	4/26 (15%)	10 (25%)	5/14 (36%)	5/26 (19%)
Thalamus	13 (33%)	10/14 (71%)	3/26 (12%) ^d	14 (35%)	10/14 (71%)	4/26 (15%) ^d
Infratentorial lesions	20 (50%)	12/14 (86%)	8/26 (31%) ^d	25 (63%)	13/14 (93%)	12/26 (46%) ^c
Brainstem total	15 (38%)	9/14 (64%)	6/26 (23%) ^b	22 (55%)	12/14 (86%)	10/26 (38%) ^c
Cerebellum total	12 (30%)	7/14 (50%)	5/26 (19%) ^a	17 (43%)	10/14 (71%)	7/26 (27%) ^c
Enhancing lesions	13/38 (34%)	9/14 (64%)	4/24 (17%) ^c	19/40 (48%)	12/14 (86%)	7/26 (27%) ^d
Solid/nodular	11/13 (85%)			18/19 (95%)		
Ring	9/13 (69%)			10/19 (53%)		
Arc	5/13 (38%)			9/19 (47%)		

MRI: magnetic resonance imaging; MS: multiple sclerosis

^{a,b,c,d} The difference is statistically significant between the Western and Asian subtypes, at *P* values of (a) *P* < 0.05, (b) *P* < 0.025, (c) *P* < 0.01, (d) *P* < 0.001

the cerebrum, cerebellum, or brainstem, were classified as having Western-type MS.

Brain and Spinal MRI

The majority of the MRI scans were acquired on a 1.5-Tesla (Magnetom Vision, Siemens A.G., Erlangen, Germany; or Signa, GE Medical Systems, Milwaukee, USA) superconducting system with a standard circularly polarised head coil, and spinal phased-array coil. A few cases were scanned on a 1.0-Tesla superconducting system (Magnetom Expert, Siemens AG, Erlangen, Germany). The MRI brain protocol included the following pulse sequences: T2-weighted turbo/fast spin echo (SE) (TR 3500-5400 ms, TE 80-120 ms, 2 NEX), fluid-attenuated inversion recovery (FLAIR) (TR 9000-11000 ms, TE 110-120 ms, IR 2200-2800 ms, 1-2 NEX), and pre- and post-gadolinium-enhanced T1-weighted SE (TR 500-640 ms, TE 9-12 ms, 2 NEX). We used a section thickness of 5 mm, slice gap of 1-1.5 mm, 192-330 x 256-512 matrix and 158-184 x 200-210 cm field of view. Most of the sequences were acquired in the axial plane, but some of the FLAIR and post-contrast scans were also acquired in the sagittal and coronal planes.

The MRI spine protocol included the following sagittal pulse sequences: T2-weighted SE (TR 3500-4700 ms, TE 91-112 ms, 2-4 NEX), and pre- and post-gadolinium-enhanced T1-weighted SE (TR 420-700 ms, TE 7.2-12 ms, 3-4 NEX). We used a sagittal section thickness of 3 mm, slice gap of 0.3-1 mm, 180-330 x 256-512 matrix and 175-338 x 200-450 cm field of view. Axial sections were performed over some areas of cord abnormality and included some of the following sequences: T2-weighted SE (TR 5000-5400 ms, TE 91-120 ms, 2-4 NEX), and pre- and

post-gadolinium enhanced T1-weighted SE (TR 400-860 ms, TE 9.1-15 ms, 2-4 NEX). We used axial section thickness of 3-4 mm, slice gap of 0.4-0.8 mm, 192-330 x 256-512 matrix and 165-225 x 200-450 cm field of view.

The MRI brain and spinal scans were evaluated for the presence and characteristics of brain and spinal lesions as detailed in Tables 1 and 2. Each scan was read by 2 neuroradiologists, and any disagreement settled by consensus. Generally, each discrete T2 and FLAIR hyperintense brain lesion was included without restriction to size. Brain lesions were considered large when they were greater than 2 cm in maximum diameter. Corpus callosal lesions were considered part of periventricular lesions. Each discernibly discrete T2-hyperintense cord lesion was counted as one separate cord lesion. The length of the cord lesions was defined in terms of the numbers of vertebral body (VB) segments they span. Specifically, note was made if the cord lesion spanned more or less than 2 VB segments in length. The extent of cross-sectional involvement of the cord lesion, and presence of enhancement were also noted.

Statistical Analysis

Chi-square test and Student’s *t*-test was used to compare the various categorical and continuous variables. To take into account multiple comparisons, we defined a *P* value of 0.01 or less to be significant, and a *P* value between 0.05 and 0.01 was considered a trend.

Results

Patients

Nine of the 49 patients with a clinical diagnosis of CDMS had previous MRI scans that were not available for review

Table 2. Comparison of MRI Spine Findings between Western and Asian Types of MS^{11,12}

MRI spine findings	First MR scan			Cumulated scans		
	Total MS (n = 40)	Western MS (n = 14)	Asian MS (n = 26)	Total MS (n = 40)	Western type (n = 14)	Asian MS (n = 26)
T2 hyperintense cord lesions	27/33 (82%)	5/8 (63%)	22/25 (88%)	29/33 (88%)	6/8 (75%)	23/25 (92%)
1 lesion only	12/27 (44.4%)	3/8 (48%)	9/25 (36%)	4/29 (13.8%)	2/8 (25%)	2/25 (8%)
2 or more lesions	15/27 (56%)	2/8 (25%)	13/25 (52%)	25/29 (86.2%)	4/8 (50%)	21/25 (84%)
Enhancing cord lesions	12/30 (40%)	3/8 (38%)	9/22 (41%)	18/32 (56%)	3/8 (38%)	15/24 (63%)
Total cord lesions	46					
• Length of T2-hyperintense lesion						
<2 VB segment	22/46 (48%)					
>2 VB segment	24/46 (52%)					
• Cross-sectional involvement						
More than half cord involved	21/46 (46%)					
Patchy or <half	25/46 (54%)					

MRI: magnetic resonance imaging; MS: multiple sclerosis; VB: vertebral body
 NB: The difference between the Western and Asian types is generally not statistically significant.

(hard copy films were lost or not in the hospital PACS), and therefore excluded from the study. Of the remaining 40 patients, 32 were female (80%) and 8 male. The racial distribution was 36 Chinese (90%), 3 Indians and 1 Malay. The mean age was 36.2 ± 14.8 years. Twenty-two patients (55%) first presented with transverse myelitis, 11 (27.5%) with optic neuritis, 4 (10%) with symptoms and signs localising to the cerebrum, and 3 (7.5%) localising to the brainstem and cerebellum. Twenty-six of the 40 patients (65%) were clinically classified as having Asian-type MS, whereas 14 patients (35%) were classified as Western-type MS. Twenty-eight patients (70%) had analysis of the cerebrospinal fluid for oligoclonal bands: 9 were positive (32.1%, $n = 28$), but 19 were negative (67.9%, $n = 28$). Of these, 6 (of 18 patients, 33.3%) had Asian-type MS and 3 (of 10 patients, 30%) had Western-type MS. Visual evoked potential (VEP) was performed in 35 patients (87.5%): this was positive in 25 patients (71.4%, $n = 35$) and negative in 10 (28.6%, $n = 35$). Of these, 15 (of 22 patients, 68.2%) had Asian-type MS and 10 (of 13 patients, 76.9%) had Western-type MS.

Brain MR Findings

All patients had MRI brain scans (mean MRI scan per patient, 3; range, 1 to 14), and a total of 119 MRI brain scans were reviewed. The time interval between the first and the last MRI scan ranged from 2.3 months to 6.7 years (mean, 2.4 years). All patients had contrast administration except for 2 on their initial brain scan. The number of patients with presence of each MRI criterion is detailed in Table 1, and some examples are illustrated in Figure 1. The McDonald MRI brain criteria found in our patients based on both the first and cumulated MRI brain scans, in descending order of frequency, are: juxtacortical lesions, periventricular lesions, infratentorial lesions, and enhancing or 9 or more T2-hyperintense lesions. The frequency of enhancing brain lesions (64% vs 17% on initial scans, $P < 0.01$, 86% versus

27% on cumulated scans, $P < 0.001$), infratentorial lesions, thalamic lesions and external capsule lesions in the Western-type MS was higher than in the Asian-type MS. These differences were statistically significant at either values of $P < 0.01$ or $P < 0.001$. There was a trend (P value between 0.05 and 0.01) towards a higher frequency of juxtacortical lesions, 9 or more T2-hyperintense lesions, corpus callosal lesions and temporal lesions on both/either of the initial and cumulated MRI in Western- than Asian-type MS. Large (>2cm) lesions and internal capsular lesions tended to be more frequent in Western-type than Asian-type MS on initial scans, and the difference achieved statistical significance ($P < 0.001$ and $P < 0.01$ respectively) on cumulated scans. The brainstem lesions were most commonly found in the pons, followed by medulla and midbrain, whilst cerebellar lesions were more common in the peduncles than hemispheres. The most common pattern of enhancement in enhancing lesions was nodular, followed by ring and arc patterns. In general, the frequency of MRI brain abnormalities in our patients was comparable to that published in the literature^{16,17} for both white and gray matter lesions, as shown in Table 3.

Spinal MR Findings

Thirty-three patients (82.5%) also had spinal MRI (mean MRI scan per patient, 2.7; range, 1 to 13), and 110 spinal MRI scans were read in total. The mean time interval between the first and the last MRI scan ranged from 1.4 months to 5.9 years (mean, 2.1 years). Three patients did not have contrast administration on their initial spine MRI ($n = 30$), and only 1 did not after cumulated scans ($n = 32$). The patient and total cord lesion count, with respect to each MR characteristic, is detailed in Table 2, with 2 patients illustrated in Figure 2. Twenty-seven patients (81.8%, $n = 33$) had cord lesions on the first MRI study, and after cumulated scans there were 29 (87.9%, $n = 33$). At first spinal MRI, 15 patients (55.6%, $n = 27$) had 2 or more

Table 3. Frequency of MRI Abnormalities in our Patients Compared to that Published in the Literature

Brain MRI findings	Our cohort on initial MRI (n = 40)	Our cohort upon cumulated MRI (n = 40)	Ormerod et al ¹⁶ (n = 114)	Noakes et al ¹⁷ (n = 42)
Juxtacortical	65%	73%	–	76%
Internal capsule	28%	43%	11%	38%
Temporal lobe	35%	58%	59%	–
Basal ganglia	18%	25%	25%	16%
Thalamus	33%	35%	34%	–
Brainstem	38%	55%	68%	48%
Cerebellum	30%	43%	49%	20%
No lesions	15%	10%	1	9.5%

MRI: magnetic resonance imaging

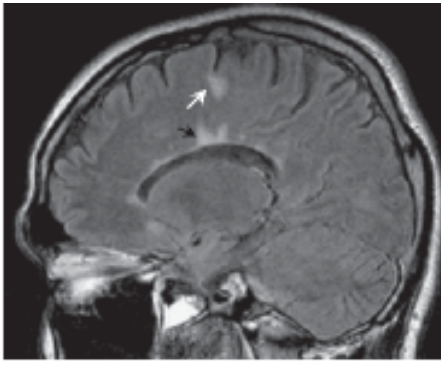


Fig. 1a.

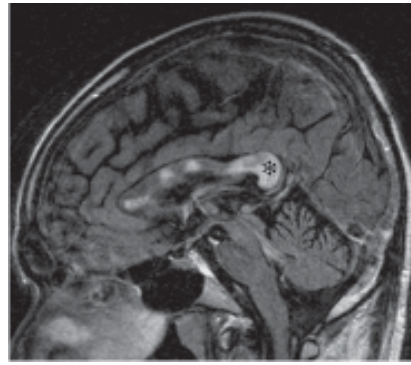


Fig. 1b.

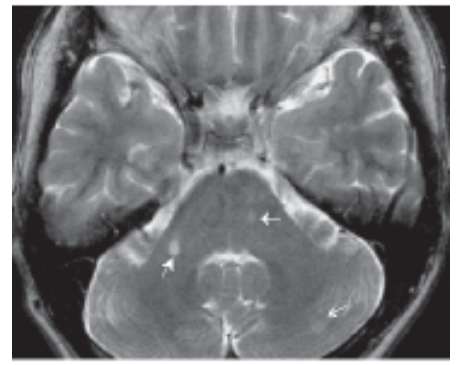


Fig. 1c.

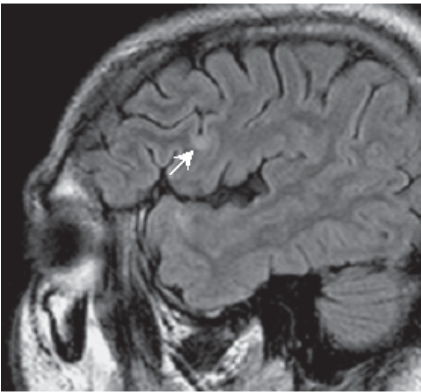


Fig. 1d.

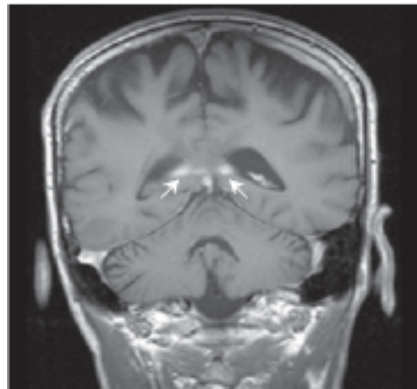


Fig. 1e.

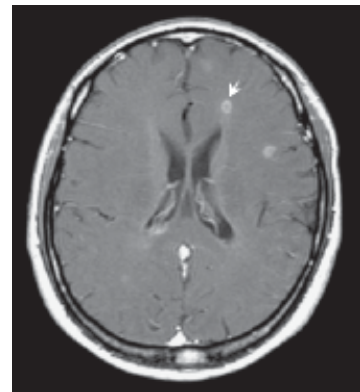


Fig. 1f.

Fig. 1. MR images from different patients in the study cohort. Typical examples of juxtacortical (white arrow) and periventricular (black arrow) MS plaques are demonstrated on sagittal FLAIR images (a) through the body of the lateral ventricle, and (b) in the midline. Note that corpus callosal plaques are considered “periventricular lesions”, and an example of a “large” plaque at the splenium (asterisk). (c) Axial T2-weighted image shows plaques at the left pons, right cerebellar peduncle and left cerebellum, and (d) sagittal FLAIR image demonstrates a cortical plaque (white arrow). Nodular and ring enhancing plaques (arrows) are shown on contrast-enhanced T1-weighted (e) coronal and (f) axial images respectively.



Fig. 2a.

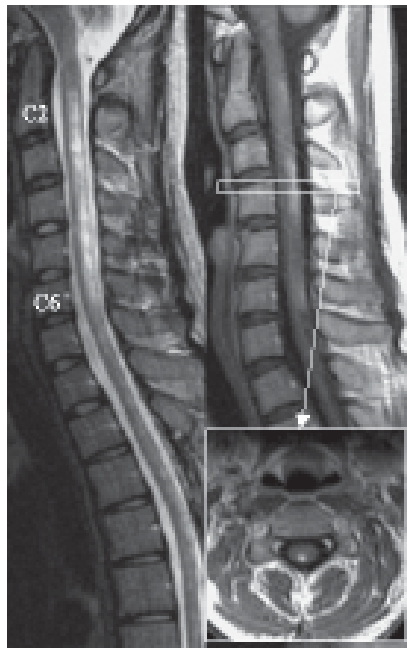


Fig. 2b.

Fig. 2. Demyelinating cord lesions of varying lengths on sagittal T2-weighted images of 2 patients, with corresponding sagittal (and axial in inset) contrast enhanced T1-weighted images. (a) Short [<2 vertebral body (VB) segments] T2-hyperintense plaques in the cord at the C2 and T1-2 levels, with patchy enhancement (arrow) in the former. (b) Long T2-hyperintense plaque spanning 5 VB segments and demonstrating patchy areas of nodular enhancement (inset).

Table 4. Comparison of Diagnostic Yield Between Western and Asian Types of MS^{11,12} When Applying McDonald's MRI Criteria⁵ for MS

McDonald MRI criteria ⁵ and MRI findings (n = 40)	First MR scan (dissemination in space)			Cumulated scans (dissemination in space)		
	Total MS (n = 14)	Western MS (n = 26)	Asian MS (n = 40)	Total MS (n = 14)	Western type (n = 26)	Asian MS
No brain lesions	6/40 (15%)	0/14 (0%)	6/26 (23%)	4/40 (10%)	0/14 (0%)	4/26 (15%)
Brain lesions present	34/40 (85%)	14/14 (100%)	20/26 (77%)	36/40 (90%)	14/14 (100%)	22/26 (85%)
McD satisfied based on brain MRI	20/40 (50%)	11/14 (79%)	9/26 (35%) ^c	25/40 (63%)	14/14 (100%)	11/26 (42%) ^d
McD not satisfied on brain MRI	20/40 (50%)	3/14 (21%)	17/26 (65%) ^c	15/40 (38%)	0/14 (0%)	15/26 (58%) ^d
No brain lesion	6/20 (30%)	0/14 (0%)	6/26 (23%)	4/15 (27%)	0/14 (0%)	4/26 (15%)
No cord lesion either	2/6 (33%)	0/14 (0%)	2/26 (8%)	1/4 (25%)	0/14 (0%)	1/26 (4%)
Brain lesion found with:	14/20 (70%)	3/14 (21%)	11/26 (42%)	11/15 (73%)	0/14 (0%)	11/26 (42%) ^c
Cord lesion, no enhancement	4/14 (29%)	1/14 (7%)	3/26 (12%)	6/11 (55%)	0/14 (0%)	6/26 (23%)
Cord lesion and enhancement	4/14 (29%)	1/14 (7%)	3/26 (12%)	2/11 (18%)	0/14 (0%)	2/26 (8%)
Inadequate despite cord findings	4/14 (29%)	0/14 (0%)	4/26 (15%)	3/11 (27%)	0/14 (0%)	3/26 (12%)
No cord lesion	2/14 (14%)	1/14 (7%)	1/26 (4%)	0/11 (0%)		
McD satisfied on brain MRI alone	20/40 (50%)	11/14 (79%)	9/26 (35%) ^c	25/40 (63%)	14/14 (100%)	11/26 (42%) ^d
McD satisfied if a cord lesion counted as 1 criterion met	24/40 (60%)	12/14 (86%)	12/26 (46%) ^b	31/40 (78%)	14/14 (100%)	17/26 (65%) ^b
McD satisfied if an enhancing cord lesion counted as 2 criteria met	28/40 (70%)	13/14 (93%)	15/26 (58%) ^b	33/40 (83%)	14/14 (100%)	19/26 (73%) ^a

MRI: magnetic resonance imaging; MS: multiple sclerosis; McD: McDonald's criteria

^{a,b,c,d} The difference is statistically significant between the Western and Asian subtypes, at *P* values of (a) *P* < 0.05, (b) *P* < 0.025, (c) *P* < 0.01, (d) *P* < 0.001

discrete cord lesions. The few patients who did not have contrast administration on their MRI spine scans all had T2-hyperintense cord lesions. About half of the patients who had contrast-enhanced spine MRI scans showed enhancing cord lesions. A patchy pattern of enhancement was the most common. Solid and ring enhancements were also seen in 5 and 3 patients respectively (27.8% and 16.7% respectively, *n* = 18) upon cumulated scans. Of 46 total cord lesions found on first spinal MRI, slightly more than half (52.2%) were longer than 2 VB segments in length, and the majority involved less than half of the cross-section of the cord.

Sensitivity of McDonald's MRI Criteria

The differences in sensitivity between Western- and Asian-type MS when applying the McDonald's MRI criteria on our patient cohort are tabulated in Table 4. Twenty (50%) patients satisfied the McDonald MRI criteria based on the first MRI brain scan alone, with 5 more doing so upon accumulated MRI brain scans (*n* = 25, 63%). If the presence of a cord lesion was considered as 1 of 3 McDonald's MRI criteria, there were 24 patients (60%) and 31 patients (78%) who would have satisfied McDonald's MRI criteria at first and cumulated scans respectively. Alternatively, if the MRI criterion of at least 1 enhancing

lesion was expanded to include enhancing cord lesions, i.e., the presence of a cord lesion showing gadolinium-enhancement was interpreted as satisfying 2 out of the 3 McDonald's MRI criteria, then the figure further increased to 28 patients (70%) and 33 patients (83%), respectively. Notably, the difference in sensitivity when applying the McDonald's MRI criteria for MS between Western- and Asian-type MS was statistically significant at the initial MRI scan (*P* < 0.01), and further increased (*P* < 0.001) upon cumulated MRI, when based upon MRI brain findings alone. In addition, when cord lesions were included either as satisfying 1 or 2 of 3 McDonald's MRI criteria, there remained a trend of higher diagnostic yield (*P* value between 0.025 and 0.01) when applied on the Western-type MS patients than on the Asian-type MS patients.

Discussion

The majority (65%) of our patients comprised the Asian-type MS phenotype. Generally, the frequency of MRI findings in our patient cohort is similar to that found in the literature (Table 3).^{16,17} Interestingly, although Brownell and Hughes¹⁸ found only 9% of total MS plaque load localised to the cortex (5%) and central gray matter (4%), the frequency of basal ganglionic (16% to 25%) and thalamic (34%) involvement by plaques in MS patients is

not minuscule (Table 3).^{16,17} Previous pathologic studies had shown that all parts of the cerebrum were vulnerable to plaque formation to some degree,¹⁸ including the gray matter. Small cortical MS lesions are also commonly found neuro-pathologically, but under-reported on MRI.¹⁹ Undoubtedly, an increased awareness of MS plaque involvement in gray matter, improvements in spatial resolution in MRI technology and the liberal use of FLAIR and contrast-enhanced scans could increase the pick-up of such lesions. More importantly, the presence of lesions in the gray matter does not exclude the diagnosis of MS.²⁰

Notably, slightly more patients met the criterion of having “a juxtacortical lesion” than the more familiar “three or more periventricular lesions” criterion. This is not surprising since juxtacortical lesions and enhancing lesions were found to be more specific MRI criteria for MS than periventricular or infratentorial lesions.⁴ Similar to a Japanese study,¹¹ statistically significant differences in MRI findings were found between the Asian- and Western-type MS in our cohort. In comparison to Western-type MS, fewer gadolinium-enhancing brain lesions, and infratentorial, thalamic and external capsular lesions characterise the Asian-type MS. This was also true of large lesions and internal capsular lesions on cumulated scans. These MRI findings lend further support to the belief that MS in Asians presents as 2 distinctive phenotypic expressions of a single disease.^{11,12}

The frequency of T2-hyperintense cord lesions and gadolinium-enhancing lesions was higher in the Asian than in the Western type, although the difference did not reach statistical significance. This could be due to the relatively small sample size of positive cases in the Western-type MS group. In contrast to the study by Tartaglino et al,²¹ we found a slight dominance of T2-hyperintense cord lesions that were longer than 2 VB segments in length. Although not statistically significant between the Asian and Western types, cord lesions were also previously noted by Kira et al¹¹ to be longer in the Asian-type than in the Western-type MS. Also, separate but subjacent cord lesions might not be readily resolved as discrete based on sagittal sections.

For the purposes of this study, we included all T2 and FLAIR hyperintense brain lesions without size restriction. This is because it is not uncommon for patients from this part of the world to delay seeking medical attention or doctor-hop. We saw lesions less than 3 mm in size that were clearly chronic plaques based on serial scans. In addition, confluent periventricular plaques raised the possibility of underestimation of the number of lesions. Whilst we recognise that Barkhof’s criteria⁴ (from whence McDonald’s MRI criteria⁵ were derived) was originally conceived for the prediction of conversion to CDMS, we suspect that radiologists in countries with restricted and hence delayed

access to MRI may also encounter this size problem in trying to apply McDonald’s MRI criteria for the diagnosis of MS.

Our results showed that when using the McDonald MRI criteria⁵ based on brain findings alone, the diagnosis of MS was more likely to be made in an MS patient who presented clinically as the Western-type MS. Applying McDonald’s criteria, for example, a single juxtacortical brain lesion that also enhanced with gadolinium would have readily met 2 out of 3 of McDonald’s MRI criteria. However, the McDonald’s MRI criteria also allowed for “substitution of one brain for a spinal lesion”.⁵ If this was interpreted to say the same for an enhancing spinal cord lesion, as it is for a single enhancing juxtacortical brain lesion, the diagnostic yield in our patient cohort could be improved by 1.4 times (from 50% to 70% or 63% to 83% on initial or cumulated MRI scans) by substituting 2 brain criteria with 2 spinal criteria. Our findings suggest that if the provision for substitution of “one brain for a spinal lesion” in McDonald’s MRI criteria could be interpreted in this fashion, there could be significant impact on the diagnosis of MS in patients presenting clinically with the Asian-type MS phenotype, with consequences on their subsequent management. This is especially so since there is preponderance of spinal lesion load in Asian-type MS.¹¹

Clearly, there is a need for a prospective study to evaluate the usefulness of McDonald’s criteria in predicting conversion to CDMS in an Asian cohort, and to assess if modifications in the interpretation of McDonald’s MRI criteria as suggested by this study could optimise its sensitivity and specificity. Certainly, the diagnostic pick-up could be further improved when the McDonald’s MRI criteria were applied in conjunction with the cerebrospinal fluid (CSF) analysis and VEP results (findings that are normally less readily available to the radiologist).

Conclusion

In summary, to our knowledge, this is the first study evaluating the utility of the McDonald criteria in MRI on a group of Asian patients with CDMS. Our study shows that there are significant MRI differences in the Western- and Asian-type MS, supporting the validity of the clinical classification of the Western and Asian types of MS. The provision for substitution of brain lesions by spine lesions as proposed by the International Panel on MS Diagnosis⁵ is helpful in Asian patients, where there is generally a higher prevalence of cord lesions. In addition, our findings suggest that minor modifications in the interpretation of the McDonald’s MRI criteria when applied to patients clinically presenting as Asian-MS could impact its sensitivity and thence patient’s subsequent treatment.

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REFERENCES

1. Paty DW, Oger JJ, Kastrukoff LF, Hashimoto SA, Hooge JP, Eisen AA, et al. MRI in the diagnosis of MS: a prospective study with comparison of clinical evaluation, evoked potentials, oligoclonal banding and CT. *Neurology* 1988;38:180-5.
2. Fazekas F, Barkhof F, Filippi M, Grossman RI, Li DK, McDonald WI, et al. The contribution of magnetic resonance imaging to the diagnosis of multiple sclerosis. *Neurology* 1999;53:448-56.
3. Fazekas F, Offenbacher H, Fuchs S, Schmidt R, Niederkorn K, Horner S, et al. Criteria for an increased specificity of MRI interpretation in elderly subjects with suspected multiple sclerosis. *Neurology* 1988;38:1822-5.
4. Barkhof F, Filippi M, Miller DH, Scheltens P, Campi A, Polman CH, et al. Comparison of MRI criteria at first presentation to predict conversion to clinically definite multiple sclerosis. *Brain* 1997;120:2059-69.
5. McDonald WI, Compston A, Edan G, Goodkin D, Hartung HP, Lublin FD, et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the Diagnosis of multiple sclerosis. *Ann Neurol* 2001;50:121-7.
6. Tintore M, Rovira A, Brieva L, Grive E, Jardi R, Borrás C, et al. Isolated demyelinating syndromes: comparison of CSF oligoclonal bands and different MR imaging criteria to predict conversion to CDMS. *Mult Scler* 2001;7:359-63.
7. Tintore M, Rovira A, Rio J, Nos C, Grive E, Sastre-Garriga J, et al. New diagnostic criteria for multiple sclerosis: application in first demyelinating episode. *Neurology* 2003;60:27-30.
8. Dalton CM, Brex PA, Miszkiel KA, Hickman SJ, MacManus DG, Plant GT, et al. Application of the new McDonald criteria to patients with clinically isolated syndromes suggestive of multiple sclerosis. *Ann Neurol* 2002;52:47-53.
9. Hahn CD, Shroff MM, Blaser SI, Banwell BL. MRI criteria for multiple sclerosis: evaluation in a pediatric cohort. *Neurology* 2004;62:806-8.
10. Bot JC, Barkhof F, Polman CH, Lycklama a Nijeholt GJ, de Groot V, Bergers E, et al. Spinal cord abnormalities in recently diagnosed MS patients. Added value of spinal MRI examination. *Neurology* 2004;62:226-33.
11. Kira J, Kanai T, Nishimura Y, Yamasaki K, Matsushita S, Kawano Y, et al. Western versus Asian types of multiple sclerosis: immunogenetically and clinically distinct disorders. *Ann Neurol* 1996;40:569-74.
12. Kuroiwa Y, Igata A, Itahara K, Koshijima S, Tsubaki T. Nationwide survey of multiple sclerosis in Japan. Clinical analysis of 1,084 cases. *Neurology* 1975;25:845-51.
13. Das A, Puvanendran K. A retrospective review of patients with clinically definite multiple sclerosis. *Ann Acad Med Singapore* 1998;27:204-9.
14. Goodin DS, Frohman EM, Garmany GP Jr, Halper J, Likosky WH, Lublin FD, et al; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Disease modifying therapies in multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology* 2002;58:169-78.
15. Poser CM, Paty DW, Scheinberg L, McDonald WI, Davis FA, Ebers GC, et al. New diagnostic criteria for multiple sclerosis: guidelines for research protocols. *Ann Neurol* 1983;13:227-31.
16. Ormerod IE, Miller DH, McDonald WI, du Boulay EP, Rudge P, Kendall BE, et al. The role of NMR imaging in the assessment of multiple sclerosis and isolated neurological lesions. A quantitative study. *Brain* 1987;110:1579-616.
17. Noakes JB, Herkes GK, Frith JA, McLeod JG, Jones MP. Magnetic resonance imaging in clinically-definite multiple sclerosis. *Med J Aust* 1990;152:136-40.
18. Brownell B, Hughes JT. The distribution of plaques in the cerebrum in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1962;25:315-20.
19. Kidd D, Barkhof F, McConnell R, Algra PR, Allen IV, Revesz T. Cortical lesions in multiple sclerosis. *Brain* 1999;122:17-26.
20. Baum PA, Barkovich AJ, Koch TK, Berg BO. Deep gray matter involvement in children with acute disseminated encephalomyelitis. *AJNR Am J Neuroradiol* 1994;15:1275-83.
21. Tartaglino LM, Friedman DP, Flanders AE, Lublin FD, Knobler RL, Liem M. Multiple sclerosis in the spinal cord: MR appearance and correlation with clinical parameters. *Radiology* 1995;195:725-32.